

CARDIOVASCULAR MEDICINE

Staphylococcus lugdunensis infective endocarditis: description of 10 cases and analysis of native valve, prosthetic valve, and pacemaker lead endocarditis clinical profiles

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Objective: To evaluate the incidence and the clinical and echocardiographic features of infective endocarditis (IE) caused by *Staphylococcus lugdunensis* and to identify the prognostic factors of surgery and mortality in this disease.

Design: Prospective cohort study.

Setting: Study at two centres (a tertiary care centre and a community hospital).

Patients: 10 patients with IE caused by *S lugdunensis* in 912 consecutive patients with IE between 1990 and 2003.

Methods: Prospective study of consecutive patients carried out by the multidisciplinary team for diagnosis and treatment of IE from the study institutions. English, French, and Spanish literature was searched by computer under the terms "endocarditis" and "*Staphylococcus lugdunensis*" published between 1989 and December 2003.

Main outcome measures: Patient characteristics, echocardiographic findings, required surgery, and prognostic factors of mortality in left sided cases of IE.

Results: 10 cases of IE caused by *S lugdunensis* were identified at our institutions, representing 0.8% (four of 467), 1.5% (two of 135), and 7.8% (four of 51) of cases of native valve, prosthetic valve, and pacemaker lead endocarditis in the non-drug misusers. Native valve IE was present in four patients (two aortic, one mitral, and one pulmonary), prosthetic valve aortic IE in two patients, and pacemaker lead IE in the other four patients. All patients with left sided IE had serious complications (heart failure, periannular abscess formation, or shock) requiring surgery in 60% (three of five patients) of cases with an overall mortality rate of 80% (four of five patients). All patients with pacemaker IE underwent combined medical treatment and surgery, and mortality was 25% (one patient). In total 59 cases of IE caused by *S lugdunensis* were identified in a review of the literature. The combined analysis of these 69 cases showed that native valve IE (53 patients, 77%) is characterised by mitral valve involvement and frequent complications such as heart failure, abscess formation, and embolism. Surgery was needed in 51% of cases and mortality was 42%. Prosthetic valve endocarditis (nine of 60, 13%) predominated in the aortic position and was associated with abscess formation, required surgery, and high mortality (78%). Pacemaker lead IE (seven of 69, 10%) is associated with a better prognosis when antibiotic treatment is combined with surgery.

Conclusions: *S lugdunensis* IE is an uncommon cause of IE, involving mainly native left sided valves, and it is characterised by an aggressive clinical course. Mortality in left sided native valve IE is high but the prognosis has improved in recent years. Surgery has improved survival in left sided IE and, therefore, early surgery should always be considered. Prosthetic valve *S lugdunensis* IE carries an ominous prognosis.

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Staphylococci species constitute a very important group of pathogens in infections of the cardiovascular system. The pathogenic significance and aggressiveness of these bacteria are well known.¹ *Staphylococcus lugdunensis* was initially described in 1988² as a separate species of coagulase negative staphylococci. The pathogenic potential of this microorganism has been clarified in a number of publications describing predominantly infections of the skin and soft tissues.³ In contrast to other staphylococcal endocarditis, infective endocarditis (IE) caused by *S lugdunensis* has seldom been reported in the past, and only case reports and brief case series have been published.⁴⁻⁴³ In this report we describe our prospective experience with 10 new cases of IE caused by *S lugdunensis*. In addition, we have extensively reviewed the

literature with the goal of providing more insight into the incidence and the clinical and echocardiographic features of IE caused by *S lugdunensis*, and the prognostic factors for requiring surgery and mortality in this disease.

PATIENTS AND METHODS

Patient population

This prospective study of consecutive patients was carried out by the multidisciplinary team for diagnosis and treatment of IE from the Hospital Clinic of Barcelona and the Infectious Diseases Unit from Mútua de Terrassa Hospital. The study institutions are a tertiary referral centre for complicated endocarditis and a community hospital, respectively, with a catchment area of 1 050 000 inhabitants.

We prospectively identified and followed up all patients with IE admitted to both hospitals between 1990 and December 2003. Data were collected prospectively with a previously designed questionnaire that specified the clinical, microbiological, echocardiographic, treatment, and outcome variables.⁴⁴ Diagnosis of IE was established according to the Duke criteria.⁴⁵ Results of two dimensional transthoracic echocardiography were routinely evaluated in all patients. Transoesophageal echocardiography was performed for suspected left sided endocarditis poorly defined by transthoracic echocardiography and for suspected intracardiac complications (complicated IE) and in all cases of prosthetic valve endocarditis.

Microbiology

All isolates of coagulase negative staphylococci are routinely sent for speciation at our institutions. *S. lugdunensis* has been prospectively identified since 1996. All specimens of IE have been prospectively collected since 1990 and coagulase negative staphylococci were retrospectively investigated to identify all isolates of *S. lugdunensis* from the study institutions.

S. lugdunensis is a coagulase negative staphylococcus that can be identified with considerable accuracy according to its positive ornithine decarboxylase activity. All strains isolated were identified as *S. lugdunensis* on the basis of the following phenotypic characteristics: coagulase negative, pyrrolidonyl arylamidase positive, production of acetoin from glucose or pyruvate, and production of acid from trehalose, mannose, maltose, lactose, sucrose, and *N*-acetyl-glucosamide.⁴⁶ A commercial identification system (Api ID32 Staph, bioMérieux, Marcy l'Etoile, France) was used. Susceptibility to antimicrobial agents was determined by a disk diffusion method and confirmed by a broth microdilution method. In both cases, the recommendations stated in the National Committee for Clinical Laboratory Standards were followed.⁴⁷

Literature review

The English, French, and Spanish language literature from 1988 to December 2003 was searched by computer (Medline) with the keywords "endocarditis" and "*Staphylococcus lugdunensis*".

Statistical analysis

Data were processed with the BMDP (1990) statistical package (BMDP Statistical Software, Inc, Los Angeles, California, USA). Clinical and echocardiographic variables for patients who required surgical treatment and for those with adverse outcome were analysed with Student's *t* test for continuous variables and Fisher's exact test for categorical variables. The relation between covariates and requiring surgery or mortality was assessed by univariate analysis. Odds ratios (OR) were then determined with a logistic regression model. The OR and 95% confidence intervals (CI) were calculated by StataCorp 1999 (Stata Statistical Software, release 6.0; Stata Corporation, College Station, Texas, USA). An adjusted analysis was performed with models constructed by multiple logistic regression analysis. Differences were considered significant when two sided *p* was less than 0.05.

RESULTS

Patient characteristics

IE was diagnosed in 912 consecutive patients between 1990 and December 2003 in the study institutions; 259 cases of IE were in injection drug users and 653 in the general population. Ten cases of IE caused by *S. lugdunensis* were identified at the study institutions representing 1.1% of all cases of IE, and 0.8%, 1.5%, and 7.8% of patients with native valve, prosthetic valve, and pacemaker lead endocarditis,

Table 1 Cases of infective endocarditis (IE) diagnosed from 1990 to 2003 at both study institutions

	Overall	Cases caused by <i>S. lugdunensis</i>
Injection drug users	259	0 (0%)
General population	653	10 (1.5%)
Native valve IE	467	4 (0.8%)
Prosthetic valve IE	135	2 (1.5%)
Pacemaker lead IE	51	4 (7.8%)
Total	912	10 (1.1%)

respectively, in non-drug misusers (table 1). Table 2 summarises clinical variables and outcome of patients from the study institutions. Four patients had native valve IE (two aortic, one mitral, and one pulmonary), two had prosthetic valve aortic infection, and four had pacemaker lead endocarditis. All three patients with left sided native valve IE had serious complications (heart failure, periannular abscess formation, or shock) and two patients underwent surgery but died. Endocarditis was diagnosed in the remaining patient at necropsy. Prosthetic valve endocarditis was found in two patients, both in the aortic position and both complicated by periannular abscess formation; one patient underwent surgery and one patient died. All four patients with pacemaker lead endocarditis (three DDD and one VVI pacemaker) underwent combined medical treatment and surgery (complete removal of the pacing system) and mortality in this subgroup was 25%.

Table 3 shows surgical rates and mortality according to the staphylococcus species identified among all cases of staphylococcal endocarditis diagnosed at the study institutions from 1990 to 2003. Rates of surgery for *S. lugdunensis* IE were higher than for IE caused by *Staphylococcus aureus* in the general population (70% v 36.9%, OR 3.9, 95% CI 1.1 to 14.7) but not higher than for *Staphylococcus epidermidis* IE (70% v 60%, OR 1.5, 95% CI 0.3 to 10.0). Mortality in *S. lugdunensis* IE was higher than in *S. aureus* IE in the general population (50% v 14.5%, OR 5.9, 95% CI 1.6 to 21.2) and in *S. epidermidis* IE (50% v 20%, OR 4, 95% CI 1.1 to 14.9).

S. lugdunensis IE was identified in 59 cases of IE from 40 articles in a comprehensive review of the literature from 1988 (initial description) up to December 2003.⁵⁻⁴⁴ Table 4 shows the combined analysis of the reported cases in the literature and those from our institutions (69 cases). Native valve, prosthetic valve, and pacemaker IE accounted for 77%, 13%, and 10% of cases from the overall population. Native valve IE (77% of cases) was characterised by mitral valve involvement (55%), acute onset (54%), and frequent complications such as heart failure (45%), periannular abscess formation (19%), and peripheral embolism (30%). Surgery was performed in 51% of patients; mortality was 42% in the overall group and 29% in patients who underwent surgery. In native valve disease, surgery was associated with improved survival (OR 3.2, 95% CI 1.1 to 8.9). Prosthetic valve endocarditis (13% of cases) predominated in the aortic position (77%) and was associated with extensive periannular tissue destruction (abscess formation in 66% of cases). In this subgroup of patients, surgery was performed in 55% and mortality was 78%. Pacemaker lead IE (10% of cases) was associated with a benign prognosis. Antibiotic treatment combined with surgery (extraction of all infected hardware) resulted in a mortality of 14%.

Antibiotic treatment

Data on antibiotic susceptibility were obtained for 71% of patients; 84% of strains were penicillin susceptible, 94% were

Table 2 Clinical characteristics, management, and outcome of patients from the two institutions

Age (years)	Sex	Co-morbidity	Valve involved, clinical presentation	Complications	Surgery	Outcome
77	F	Liver cirrhosis, Le Veen shunt	Native mitral, acute, no echocardiography	Meningitis, CHF	No	Died in hospital
82	F	Ischaemic heart disease	Native atrial, acute, veg 12 mm	AMI, CHF, periannular abscess	Yes	Died in hospital
68*	F	DDD pacemaker 7 years, battery replacement 1 year previously	Pacemaker lead veg 22 mm, early onset	None	Yes	Alive; relapse 1 year after initial medical treatment: delayed surgery (ET)
66	M	DDD pacemaker 10 years previously	Pacemaker lead veg 23 mm, late onset	Shock	Yes (CPB)	Died in hospital
78	M	DDD pacemaker 5 years, battery replacement 4 months previously, chronic pocket infection	Pacemaker lead veg 10 mm, early onset	None	Yes (ET)	Alive
70	M	Aortic valve surgery	Aortic bioprosthesis, acute, veg 8 mm	Periannular abscess, shock	Yes	Died in hospital
77	M	Aortic valve surgery	Aortic bioprosthesis, chronic, no vegetation	Periannular abscess	No	Alive
43	F	Congenital pulmonary stenosis	Native pulmonary, acute, no veg	None	No	Alive
37	M	None	Native aortic, acute, no veg	Peripheral embolism, periannular abscess, CHF, shock	Yes	Died in hospital
63	M	VVI pacemaker 15 years, battery replacement 2 months previously, chronic pocket infection	Pacemaker lead veg 8 mm, early onset	None	Yes (ET)	Alive

*Reported previously in reference 24.

Acute, duration of symptoms ≤ 30 days; AMI, acute myocardial infarction; CHF, congestive heart failure; chronic, duration of symptoms >30 days; CPB, cardiopulmonary bypass; early onset, symptoms ≤ 12 months after surgical manipulation; ET, external traction; late onset, symptoms >12 months after surgical manipulation; F, female; M, male; Veg, vegetation.

methicillin susceptible, and all isolates were susceptible to vancomycin, aminoglycosides, and rifampin. Data on antibiotic treatment were obtained for 81% of patients and for the remaining patients antibiotic treatment was not specified. β lactams alone (seven patients) or combined with other antibiotics (aminoglycosides in 27, rifampin in one, or cephalosporins in one) were administered to 36 patients. Vancomycin alone (five patients) or combined with other antibiotics (aminoglycosides in eight, rifampin in two, cephalosporins in four, or imipenem in one) was administered to 20 patients. Differences in mortality between the antibiotic regimens were not significant (β lactams alone or combined with other antibiotics versus vancomycin alone or combined with other antibiotics, 52% *v* 35.5%, $p = 0.35$).

Required surgery in left sided endocarditis

Table 5 shows predictors of required surgery in left sided endocarditis in the univariate analysis. Younger patients (age < 50 years), absence of significant co-morbidity, aortic valve involvement, and endocarditis complicated by formation of periannular abscesses were significantly associated with

increased need for surgery. There was a trend towards increased use of surgery in multivalvar IE and when the clinical course was complicated with heart failure (table 5). All the variables in the univariate analysis with $p < 0.1$ were considered for multivariate analysis. Periannular abscess formation (OR 5.4, 95% CI 1.2 to 23.4, $p = 0.02$) and younger age (OR 4.9, 95% CI 1.3 to 18.9, $p = 0.01$) were found to be independent prognostic factors for surgery.

Prognostic factors of mortality in left sided endocarditis

Table 6 shows predictors of mortality in left sided endocarditis in the univariate analysis. Age ≥ 50 years, cases reported before 1995, and absence of surgery were significantly associated with increased mortality. Patients who did not undergo surgery had a relative risk of mortality 2.9 times (95% CI 1.0 to 8.7, $p = 0.05$) higher than those who were operated on. All the variables in the univariate analysis with $p < 0.1$ were considered for multivariate analysis. A diagnosis before 1995 (year of publication) (OR 3.3, 95% CI 1.1 to 11.4, $p = 0.05$) was the only independent prognostic factor for mortality.

DISCUSSION

The various species of coagulase negative staphylococci constitute the major component of the saprophyte flora in humans. Although multiple species of coagulase negative staphylococci have been described, only a minority infect humans but they are the leading cause of prosthetic material infection.¹ In 1988, a new genomic species of coagulase negative staphylococci was reported by Freney *et al.*² This species is readily differentiated from other coagulase negative staphylococci by the production of ornithine decarboxylase and pyrrolidonyl arylamidases. *S. lugdunensis* can bind vitronectin and fibrinogen to extracellular matrix proteins and may be misidentified as *S. aureus* because some isolates produce clumping factor, resulting in positive slide coagulase or latex agglutination tests. This may explain the disparity between *S. lugdunensis* isolates in coagulase negative staphylococci

Table 3 Surgical rates and mortality according to the staphylococcus species identified among all cases of staphylococcal endocarditis diagnosed at the study institutions (1990–2003)

	Total	Surgery	Mortality
<i>Staphylococcus aureus</i>	310	63 (20.3%)	22 (7.1%)
Injected drug users	172	12 (7.0%)	2 (1.1%)
General population	138	51 (36.9%)	20 (14.5%)
Coagulase negative staphylococci	98	53 (54.0%)	23 (23.5%)
<i>S. epidermidis</i>	75	45 (60.0%)	15 (20.0%)
<i>S. lugdunensis</i>	10	7 (70.0%)*	5 (50.0%)†
<i>S. hominis</i>	6	1 (16.6%)	1 (16.6%)
Other species	7	2 (40.0%)	1 (14.2%)

* $p < 0.04$ versus *S. aureus* in the general population and not significant versus *S. epidermidis*; † $p < 0.01$ versus *S. aureus* in the general population and $p < 0.04$ versus *S. epidermidis*.

Table 4 Overall clinical characteristics of 69 cases (10 from the two study institutions and 59 from the literature)

Clinical characteristics	Native valve (n = 53)	Prosthetic valve (n = 9)	Pacemaker lead* (n = 7)
Mean age (years)	55	63	63
Age <50 years	36%	11%	14%
Male sex	49%	33%	14%
Published before 1995	36%	77%	0%
Previous heart disease†	38%	100%	100%
Co-morbidity‡	30%	22%	14%
Known source of infection§	45%	33%	71%
Injection drug users	0%	0%	0%
Location			
Mitral valve	55%	11%	0%
Aortic valve	28%	77%	0%
Tricuspid valve	0%	0%	0%
Pulmonary valve	4%	0%	0%
Pacemaker lead	0%	0%	100%
Multivalvar	13%	11%	0%
Acute onset (≤ 30 days)	54%	11%	57%
Complications	60%	77%	14%
Heart failure	45%	22%	0%
Periannular abscess	19%	66%	0%
Embolisation	30%	11%	14%
Vegetation on echocardiogram	85%	22%	100%
Surgery	51%	55%	100%
Death	42%	78%	14%
Antibiotic + surgery	29%	80%	14%
Antibiotic alone (no surgery)	57%*¶	75%**	0%

*Pacemaker (6), implantable cardioverter defibrillator (1); †aortic (7) or mitral (1) prosthesis, rheumatic valve (6), bicuspid aortic valve (3), mitral regurgitation (6), pacemaker (6), ischaemic heart disease (2), pulmonary stenosis (1), implantable defibrillator (1); ‡AIDS (1), congestive heart failure (6), end stage renal disease (3), liver cirrhosis (2), malignancy (2), rheumatoid arthritis (2), diabetes mellitus (1), lymphoma (1), renal transplant (1); §cutaneous infection (14), arteriovenous fistula or graft (5), vasectomy (4), arthritis (2), dental abscess (1), scrotal ulceration (1), coronary angiography (1) or angioplasty (1), percutaneous valvoplasty (1), others (2); ¶p<0.04 versus antibiotic + surgery; **not significant versus antibiotic + surgery.

endocarditis, which has been reported to be between 0%⁸ and 44%.³² It may also explain why endocarditis caused by coagulase negative staphylococci is associated with a

subacute and indolent infection with few complications in some reports⁴⁸ and with an aggressive infection with valve dysfunction, heart failure, and high mortality in others.⁴⁹

Table 5 Required surgery for left sided endocarditis caused by *S. lugdunensis* (univariate analysis of episodes reported between 1988 and 2003 plus cases from the study institutions)

Variable	n	Surgery required	OR (95% CI)	p Value
Age				
≥50 years	38	17 (45%)	1	0.01
<50 years	19	15 (79%)	4.6 (1.2 to 16.5)	
Sex				
F	25	15 (60%)	1	0.6
M	32	17 (53%)	0.7 (0.2 to 2.2)	
Previous heart disease*				
No	32	17 (53%)	1	0.6
Yes	25	15 (60%)	1.3 (0.4 to 3.8)	
Co-morbidity*				
No	41	27 (66%)	1	0.02
Yes	16	5 (31%)	0.2 (0.07 to 0.8)	
Source of infection*				
Unknown	33	19 (57%)	1	0.8
Known	24	13 (54%)	0.9 (0.3 to 2.5)	
Endocarditic valve				
Prosthetic	8	5 (62%)	1	0.7
Native	49	27 (55%)	0.7 (0.1 to 3.4)	
Valve involved				
Mitral	28	10 (36%)	1	0.003
Aortic†	29	22 (76%)	5.6 (1.8 to 17.8)	
Number of valves				
1	49	26 (53%)	1	0.2
>1	8	6 (75%)	2.6 (0.5 to 14.4)	
Acute onset (≤ 30 days)				
No	10	6 (60%)	1	0.6
Yes	28	19 (68%)	1.4 (0.3 to 6.2)	
Embolisation				
No	29	16 (55%)	1	0.3
Yes	17	12 (70%)	1.9 (0.5 to 6.9)	
Diagnosis‡				
<1995	22	11 (50%)	1	0.5
≥1995	35	21 (60%)	1.5 (0.5 to 4.4)	
Periannular abscess				
No	41	19 (46%)	1	0.02
Yes	16	13 (81%)	5.0 (1.2 to 20.3)	
Heart failure				
No	20	10 (50%)	1	0.2
Yes	26	18 (69%)	2.2 (0.7 to 7.5)	

*Detailed in table 4; †includes aortic valve involvement also in multivalvar infection; ‡year of publication.

Table 6 Prognostic factors of mortality in left sided endocarditis caused by *S. lugdunensis* (univariate analysis of episodes reported between 1988 and 2003 plus cases from the study institutions)

Variable		n	Mortality	OR (95% CI)	p Value
Age	≥50 years	39	24 (61%)	1	0.01
	<50 years	19	5 (26%)	0.2 (0.06 to 0.7)	
Sex	F	26	12 (46%)	1	0.6
	M	32	17 (53%)	1.3 (0.5 to 3.7)	
Previous heart disease*	No	33	16 (48%)	1	0.8
	Yes	25	13 (52%)	1.1 (0.4 to 3.2)	
Co-morbidity*	No	42	20 (47%)	1	0.6
	Yes	16	9 (56%)	1.4 (0.4 to 4.5)	
Source of infection*	Unknown	34	19 (56%)	1	0.3
	Known	24	10 (42%)	0.5 (0.2 to 1.6)	
Endocarditic valve	Prosthetic	9	7 (77%)	1	0.08
	Native	49	22 (45%)	0.2 (0.04 to 1.2)	
Valve involved	Mitral	28	14 (50%)	1	1.0
	Aortic†	30	15 (50%)	1.0 (0.3 to 2.8)	
Number of valves	1	50	25 (50%)	1	1.0
	>1	8	4 (50%)	1.0 (0.2 to 4.4)	
Acute onset (≤30 days)	No	10	6 (60%)	1	0.2
	Yes	28	11 (39%)	0.4 (0.1 to 1.9)	
Embolisation	No	30	13 (43%)	1	0.8
	Yes	17	8 (47%)	1.2 (0.3 to 3.8)	
Diagnosis‡	<1995	23	16 (69%)	1	0.02
	≥1995	35	13 (37%)	0.2 (0.08 to 0.8)	
Periannular abscess	No	42	21 (50%)	1	1.0
	Yes	16	8 (50%)	1.0 (0.3 to 3.1)	
Heart failure	No	20	8 (40%)	1	0.7
	Yes	26	12 (46%)	1.3 (0.4 to 4.2)	
Surgery	Yes	32	12 (37%)	1	0.05
	No	25	16 (64%)	2.9 (1.0 to 8.7)	

*Detailed in table 4; †includes aortic valve involvement also in multivalvar infection; ‡year of publication.

Characteristics of *S. lugdunensis* endocarditis

S. lugdunensis is a coagulase negative staphylococcus infecting predominantly the skin and soft tissue and is only occasionally responsible for IE.³ Owing to the prospective design of this study, we calculated that *S. lugdunensis* IE accounted for only 1.1% of all cases of IE diagnosed at the study institutions, and 0.8%, 1.5%, and 7.8% cases of native valve, prosthetic valve, and pacemaker endocarditis, respectively. The majority of patients acquired the infection in the community and a site of entry was not identified for some patients. Sources of infection have been reported to be dental abscesses, cutaneous infection, infected vascular accesses, infected pacemakers, vasectomies, and others (table 4).

Some clinical determinants of *S. lugdunensis* infection have been reported previously and were confirmed in the present investigation. In contrast to the indolent presentation characteristic of native valve endocarditis caused by other coagulase negative staphylococci, *S. lugdunensis* causes valve destruction and multiple complications similar to those in endocarditis caused by *S. aureus*. *S. lugdunensis* IE is characterised by a poor response to conventional antimicrobial treatment, with important valvar destruction, myocardial abscess formation, high peripheral embolic rate, and high mortality, including cases referred for surgical treatment. The majority of cases of IE caused by *S. lugdunensis* involve native valves (77%), whereas other coagulase negative staphylococci (mainly *S. epidermidis*) infect the prosthetic valve. Mitral and aortic valve infection is often reported and in some cases there is multivalvar endocarditis. Severe complications such as heart failure and the need for valve replacement were present in 45% and 51% of patients, respectively, compared with 30–38% and 27–34% for other coagulase negative staphylococci. In line with these data, surgical rates of *S. lugdunensis* IE from all cases of staphylococcal endocarditis diagnosed at the study institutions were higher than surgical rates for *S. aureus* IE (table 3). Overall mortality is in the range

of 50%, which is considerably higher than the mortality reported for other coagulase negative staphylococci (16%).¹ As table 3 shows, we observed higher mortality for *S. lugdunensis* IE than for *S. aureus* and *S. epidermidis* IE. The higher surgical rates and mortality of *S. lugdunensis* IE are probably due to the intrinsic virulence of this particular organism. Endocarditis affected the prosthetic valve in only 13% of all cases but this type of infection is associated with the highest complication rates and mortality. Surgery did not reduce mortality in this subgroup of patients, probably because of advanced periannular destruction and the low number of patients.

Pacemaker lead endocarditis constitutes another subgroup in *S. lugdunensis* IE that has not been previously characterised. Only seven cases have been reported, three from the literature review^{22–26} and four from the present study. Pacemaker lead endocarditis accounted for 7.8% of all cases of IE from the study institutions, and when the entire pacing system was extracted mortality was very low. Mortality from electrode lead *S. lugdunensis* IE is not different from mortality caused by the general series of pacemaker lead endocarditis.⁵⁰

Antibiotic susceptibility and medical treatment

We observed no differences in terms of mortality between the treatment options. Mortality rates did not differ between treatment with β lactams alone or combined with other antibiotics and treatment with vancomycin alone or in combination, or between monotherapy and combined treatment. There is no specific pattern of susceptibility to antibiotics in endocarditis caused by *S. lugdunensis*. This makes the choice of antibiotics dependent on antibiotic susceptibility tests. However, the majority of strains were penicillin and methicillin susceptible. Despite the micro-organism's susceptibility in vitro, an antibiotic alone is seldom successful and the majority of patients need surgery during the active phase of the disease. *S. lugdunensis* and *S. aureus* share similar morphology and both species produce

clumping factor (bound coagulase) resulting in positive slide coagulase and latex agglutination test. Negative tube coagulase tests and positive pyrrolidonyl arylamidase, ornithine decarboxylase, and mannitol fermentation tests distinguish *S. lugdunensis* from other clumping factor producing staphylococcus species. Prompt speciation can lead to earlier recognition of *S. lugdunensis* and earlier suspicion of IE and, therefore, enables earlier medical treatment and surgery.

Surgery

The available clinical data suggest that *S. lugdunensis* is an aggressive pathogen. Frequent and severe in-hospital complications and high mortality characterise *S. lugdunensis* IE even when surgery is performed early in the course of the disease. Most patients had a short duration of symptoms, usually for less than three weeks, and there was often gross valvar destruction with abscess formation requiring valve replacement (table 4). In our review, 51% of patients required surgical intervention for native valve endocarditis, 55% for prosthetic infection, and 100% for infected pacemakers. Some subgroups of patients underwent surgery for left sided endocarditis to reduce mortality; 57% of patients who did not undergo surgery died compared with 29% of patients who did have surgery (table 4). Deaths were common in the older group, who were more likely treated conservatively. Absence of significant co-morbidity, aortic valve involvement, and endocarditis complicated by formation of periannular abscess were significantly associated with increased use of surgery; most deaths occurred in the earlier reports.

Prognosis

Mortality in IE caused by *S. lugdunensis* is high, both for native (42%) and prosthetic (78%) valves, although it has been shown to have decreased in recent years (year of publication after 1995). These figures are closer to those reported for IE caused by other aggressive pathogens such as *S. aureus*,⁵¹ group B streptococci,⁵² or pneumococci⁵³ and are far from the 6% mortality in non-aggressive endocarditis caused by viridans group streptococci.⁵⁴ Cases reported before 1995 and older patients (age ≥ 50 years) were significantly associated with increased mortality. Patients with left sided involvement who did not undergo an operation had a relative risk of mortality 2.9 times higher than those operated on. Although the proportion of patients referred for surgery for left sided endocarditis did not differ substantially before and after 1995 (50% v 60%, respectively), mortality decreased from 69% to 37% during both time periods. Perhaps increased recognition of this pathogen and its virulence has led to earlier and more aggressive management including surgery. Age and status of co-morbidities may have had an important role in reducing mortality because younger patients without significant co-morbidities had undergone more surgical procedures with decreased mortality. Absolute numbers of cases of prosthetic valve endocarditis caused by this organism are very low, thus precluding analysis of factors influencing mortality in prosthetic valve endocarditis. Surgical treatment was not more often required for prosthetic valve endocarditis than for native valves and surgery did not statistically reduce mortality in prosthetic valve endocarditis. This is presumed to be due to differences in baseline characteristics of patients, differences in associated complications, the aggressive nature of the infection, and the low number of patients.

Study limitations

This study has some limitations. There is a potentially significant bias because, although the study was based on a prospective analysis of cases at our institutions, the main source of information was cases reported in the literature. The severity of *S. lugdunensis* endocarditis may appear higher

because cases with a complicated course and poor outcome are more likely to be published. Subgroup analysis did not show a reduction in mortality with the use of surgery in certain subgroups of patients because of the retrospective nature of the study, and there is a clear bias in selection of the mode of treatment. A type II error due to the low number of patients is probably the cause of this lack of benefit of surgery in some subgroup of patients. However, this is the largest analysis ever reported of IE caused by *S. lugdunensis*.

Conclusion

S. lugdunensis IE is an uncommon cause of IE involving mainly native left sided valves. Despite the retrospective and non-randomised nature of the study and the potential selection bias, we conclude that *S. lugdunensis* IE has an aggressive course with high rates of severe in-hospital complications. Therefore, all coagulase negative staphylococci should be identified by species in all cases of complicated IE to allow early identification of *S. lugdunensis*. Mortality in left sided native valve endocarditis is high but the prognosis has improved in recent years. Surgery improved survival in left sided IE and, therefore, early surgery should always be considered. Prosthetic valve endocarditis due to *S. lugdunensis* carries an ominous prognosis.

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APPENDIX

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